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Congenital Hypertrichosis, Cardiomegaly and Mild Osteochondrodysplasia

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We report on a boy with congenital hypertrichosis, cardiomegaly and a mild osteochondrodysplasia, a rare syndrome of which there is only one previous report [Cantú et al., Hum Genet 60:36–41, 1982]. In all, five patients now are known to have this syndrome (2 females, 3 males). As the syndrome has been described in males and females and also in two sibs, inheritance is probably autosomal recessive. © 1996 Wiley-Liss, Inc.

KEY WORDS: congenital hypertrichosis, cardiomegaly, osteochondrodysplasia, autosomal recessive

INTRODUCTION

Cantú et al. [1982] described a new syndrome characterised by macrosomy at birth, generalised congenital hypertrichosis, coarse facial appearance, narrow thorax, cardiomegaly, wide ribs, platyspondyly, metaphyseal widening of the distal ends of the long bones, bilateral coxa valga and generalised osteopenia. This condition occurred in two affected sibs (male and female) born to non-consanguineous parents and in male and female sporadic cases; thus Cantú et al. [1982] concluded that this was an autosomal recessive trait. We describe a boy, the first in Europe with this rare autosomal recessive syndrome.

CLINICAL REPORT

The propositus was the third child of a 28-year-old mother and 30-year-old father, both healthy and non-consanguineous. The family history was unremarkable. The pregnancy was uncomplicated and ended at 40 weeks by vaginal delivery. Birth weight was 4,508 g. He was a large, profusely hirsute baby. Apart from a moderately large tongue, he was clinically normal. Initially, feeding was slow. At 8 weeks, he was admitted because of cardiomegaly. There was excessive growth of dark hair on the nape of the neck, forearms, legs and on the lumbosacral region (Fig. 1). The face (Fig. 2) was slightly coarse with hypertelorism, flared nares and a long, flat philtrum. There was an abundance of hair on the forehead which extended down the preauricular region. The eyebrows which were thick and dark were prominent laterally. The eyelashes were dark, thick and curly. The neck was short and the posterior hairline was low. The liver was 4 cm below the costal margin and the spleen was slightly enlarged. Although the heart was enlarged, the heart sounds were normal and

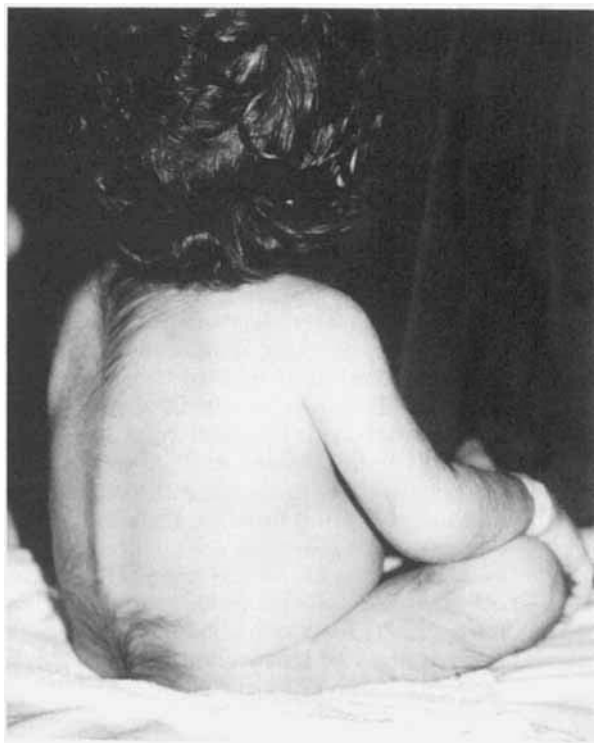

Fig. 1. Patient age 12 months with excessive hair on nape of neck, arms and legs and lumbosacral region.

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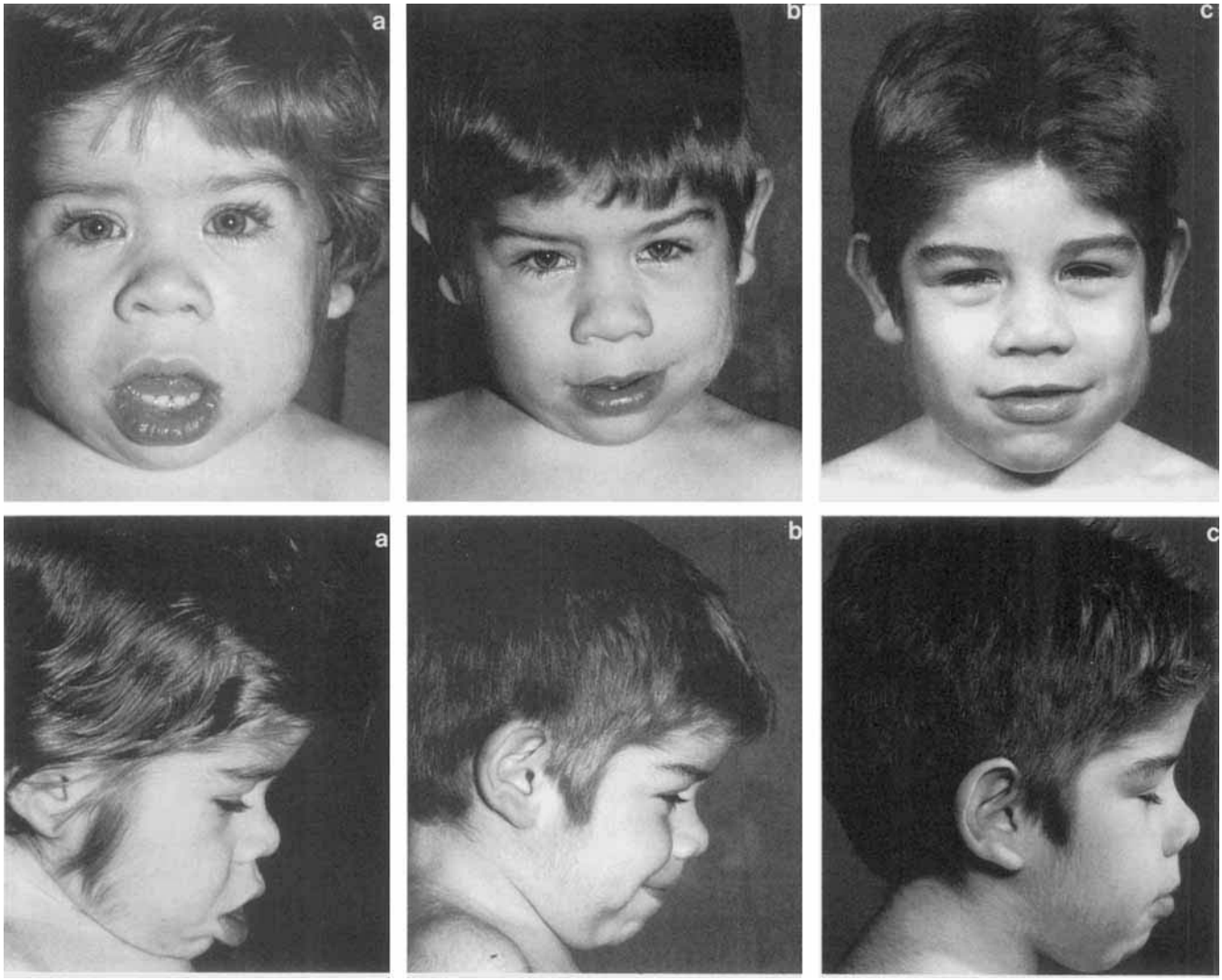

Fig. 2. Patient age 12 months (**a**), age 3 years, 8 months (**b**), and age 7 years, 10 months (**c**).

there were no murmurs. Radiology of the chest showed cardiomegaly (Fig. 3). The electrocardiogram showed a degree of right ventricular dominance. The initial clinical impression was that he had one of the mucopolysaccharidoses. However, analysis of glycosaminoglycans was normal both qualitatively and quantitatively. Culture of fibroblasts and investigation for lysosomal enzymes also were normal. Blood cell count, blood biochemistry, thyroid function tests and chromosomes were normal.

Since the age of 8 weeks, he has been followed regularly by both the paediatric cardiologist and clinical geneticist. Throughout, his height has been between the 25th and 50th centiles and his weight between the 75th and 90th centiles. The skull circumference has been just below the 98th centile. Developmentally and intellectually, he was normal.

At the age of 10 years, he developed dyspnoea on exertion. Over the previous year he had five episodes of chest infections. Clinical examination showed a grade $\frac{1}{6}$ ejection systolic murmur at the left sternal border. The chest radiograph showed cardiomegaly and pericardial effusion (Fig. 4). Since that time, he has had repeated admissions to hospital because of increasing dyspnoea and pericardial effusion. At age 14 years, he had a left anterior thoracotomy. There was pericardial thickening and a large serous effusion (Fig. 5). A pleuropericardial window was made. The biopsy of the pericardium showed pericardial fibrosis and mild focal chronic inflammation. The underlying muscle showed some degree of disorganisation. There were no inclusions in the myofibres, nor evidence of inflammation, vasculitis, recent or healed infarction. On electron microscopy there was little evidence of pathological change, apart from vacuolation in a few myofibres. The myofibres were normal. Mitochondria were numerous and normal. Endomysial collagen was not increased and there were no amyloid deposits. Age 15 years, he

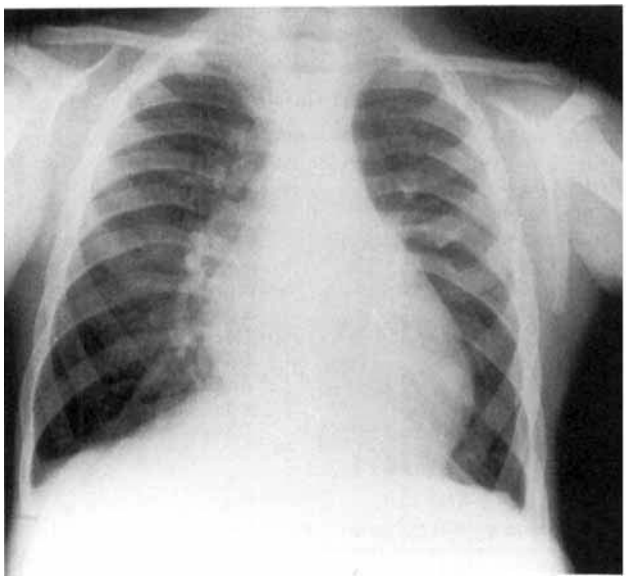

Fig. 3. Chest radiograph showing cardiomegaly and wide ribs, age 2 years, 9 months.

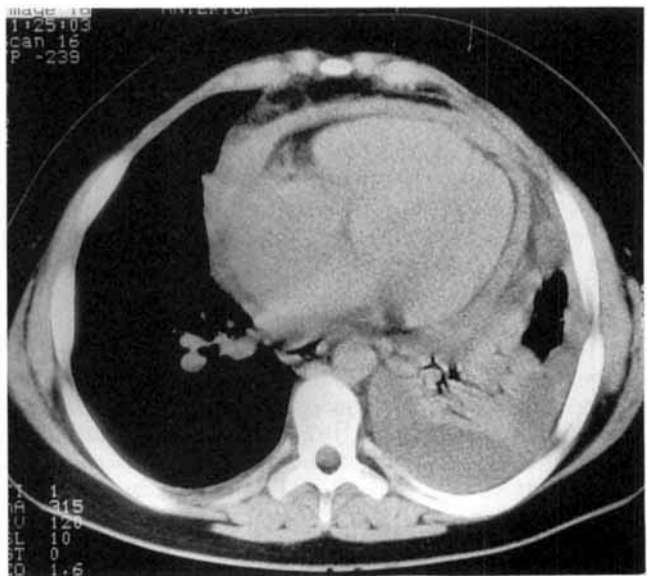

Fig. 5. CT scan showing pericardial thickening and large serous effusion.

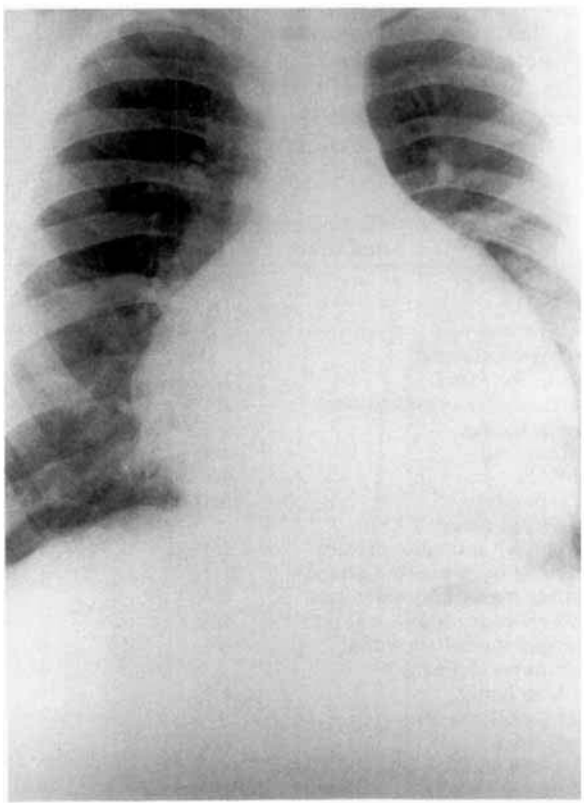

Fig. 4. Chest radiography showing pericardial effusion and cardiomegaly.

Fig. 6. Patient age 5 years showing mild flattening of the dorsal vertebrae.

complained of chest pain. There was a marked pericardial effusion. Fifty ml of fluid had been aspirated and contained pus cells. There were no signs of cardiac impairment. Echocardiography showed good function. There was a small rim of pericardial fluid. The pleural effusion increased and 900 ml of straw coloured sterile fluid was drained off. At his last review, aged 16 years, he continued to remain well. His weight was 67.6 kg. There was some dullness at the left base of the chest with diminished air entry. The chest radiograph showed left basal collapse.

RADIOLOGY

Radiographs were available for ages 2.5, 5, 12 and 14 years. The skull vault was relatively large with slight thickening mainly in the frontal region. The sella was normal, as was the base of the skull. The spine showed slight flattening of the dorsal vertebral bodies, seen best at age 5 years (Fig. 6) but still present at 14 years. There was no evidence of any irregularities of the end plates. The ribs were thick at all ages, affecting the middle and anterior thirds to a greater extent than the posterior third (Figs. 3, 4). The thoracic cage was narrow. In the early years, there was a moderate cardiac enlargement with increase in pulmonary vasculature with clear lung fields (Fig. 3). Recently, there is marked increase in the size of the cardiac silhouette due to the pericardial effusion and a left pleural effusion. The long bones which were of normal contour, were slightly shorter than normal for age. The medullary cavities between 2.5 years and 7 years were slightly wider than normal, but there was no evidence of Erlenmeyer flask deformity (Fig. 7). Radiographs of the hands and feet showed tubular bones of normal size and shape (Figs. 8, 9). Bone age was consistent with chronological age; at the age of 5 and 14 years, it was within one standard deviation of normal. The pelvis was normal (Fig. 10). There was no coxa valga.

DISCUSSION

Our patient had generalised hypertrichosis from birth, affecting head, neck, back, upper and lower arms. The appearance was consistent with hypertrichosis universalis [Beighton, 1970; Freire-Maia et al., 1976]. Usually, no other clinical abnormalities are associated with this disorder. Baumeister et al. [1993] described a Greek girl age 3 years with generalised hypertrichosis of face, ears and shoulders. The hair was fine, silky and of vellus rather than the lanugo type. This patient had a balanced pericentric inversion of 8p11.2-q22. Apart from the hypertrichosis, there were no other clinical abnormalities. Our patient and those of Cantú et al. [1982] had normal chromosomes. Wiedemann et al. [1993] report a German boy, born of non-consanguineous parents, with multiple congenital anomalies including hirsutism, marked brachycephaly, abnormal position of thumbs, pes cavus with claw toes, an abnormal face and mental retardation. He also had a uric acid metabolism disturbance. In 1982, Cantú et al. [1982] described four patients with congenital hypertrichosis, macrosomy at birth and a distinct osteochondrodysplasia and cardiomegaly. Our patient has similar clinical features and radiological findings (Tables I, II). However, the bone changes in our patient appear to be milder than those of Cantú et al.'s [1982] patients. The narrow thorax and thick ribs are similar. There are none of the changes described in the pelvis, such as hypoplasia of the ischium and pubis, small obturator foramina and coxa valga. In our patient, the only abnormalities noted in the long bones are slight shortness and thin cortices giving rise to the wide medullary cavities. The spinal changes are mild platyspondyly but with normal vertebral end plates.

The four patients of Cantú et al. [1982] had cardiomegaly. In addition to the "global cardiomegaly," one patient (case C) also had patent ductus arteriosus and

TABLE I. Review of the Clinical Findings in the Literature and in the Patient

	Cantú et al. [1982] (n = 4)	Present case
Coarse face	4/4	+[a]
Prominent forehead	1/4	−[a]
Prominent curly eyelashes	4/4	+
Epicanthal folds	3/4	−
Flat broad nasal bridge	2/4	−
Small nose	2/4	−
Hypoplastic alae nasi	2/4	−
Anteverted nares	3/4	−
Short neck	4/4	+
Narrow shoulders	4/4	+
Narrow thorax	4/4	+
Cardiomegaly	4/4	+
Cardiac anomaly	2/4	−
Umbilical hernia	2/4	−
Hepatomegaly	1/4	+
Short hands	3/4	−
Generalised hypertrichosis	4/4	+

[a] +, present; −, absent.

TABLE II. Review of Radiological Findings in the Literature and in the Patient

	Cantú et al. [1982] (n = 4)	Present case
Cranium: enlarged posterior fossa	1/4	−[a]
Cranium: more vertical base	1/4	−
Narrow thorax	4/4	+[a]
Cardiomegaly	4/4	+
Wide ribs	4/4	+
Platyspondyly	4/4	+
Vertebral bodies: irregular articular surface	1/4	−
Vertebral bodies: ovoid shape	1/4	−
Hypoplastic ischiopubic rami	4/4	−
Bilateral coxa valga	4/4	−
Enlarged medullary canal	4/4	+
Erlenmeyer deformity of long bones	4/4	−
Short distal phalanx first finger	4/4	−
Short and wide distal phalanx first toe	4/4	−
Delayed bone age	3/4	−

[a] +, present; −, absent.

Fig. 7. Patient age 4½ years, showing normal contour of long bones with widening of the medullary cavities.

Fig. 8. Patient age 15½ years, showing tubular bones of the hands of normal size and shape.

Fig. 9. Patient age 15½ years, showing normal bones of the feet.

Fig. 10. Patient age 4½ years, without hypoplasia of ischium and pubis or coxa valga.

pulmonary hypertension and another (case D) had a probable mild aortic stenosis. Our patient who had cardiomegaly has been reviewed regularly by a paediatric cardiologist (H.C.M.) since age 8 weeks. At age 8 years, he developed a pericardial effusion which over the years has increased, requiring frequent aspiration and eventually surgical intervention with the construction of a pleuropericardial window. During surgery, it was possible to undertake histological investigations. Although there was some disorganisation of the myocardium, possibly due to the overlying pericardial fibrosis, on electron microscopy, there was little evidence of myocardial pathology. There was no parental consanguinity in any of the three families described by Cantú et al. [1982]. The presence of the syndrome in a male and female in the same family suggests autosomal recessive inheritance. There was no consanguinity in the present family and two other sibs were unaffected. However, our patient confirms this syndrome as a distinct entity. Inheritance is probably in an autosomal recessive manner.

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